

B/A  
JLW



VIA HAND DELIVERY MAY 24, 2004

Docket No.: PF141P4  
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:  
Yu et al

Application No.: 09/246,129

Group Art Unit: 1647

Filed: February 8, 1999

Examiner: D. Romeo

For: Tumor Necrosis Factor-Gamma

**AMENDMENT AND SUBMISSION OF SUBSTITUTE SPECIFICATION**  
**UNDER 37 C.F.R. § 1.125**

**Mail Stop Issue Fee**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In reply to the Notice of Drawing Inconsistency with Specification mailed on May 11, 2004, in connection with the above-identified application, Applicant's submit herewith the following Amendment accompanied by: (a) a Substitute Specification containing markings to indicate changes relative to the immediate prior version; and (b) a clean version of the Substitute Specification without markings.

Applicants respectfully request entry of the following amendment.

- Amendment of the Specification begins on page 2 of this paper.
- Remarks begin on page 22 of this paper.

Okay to  
enter AR 7/27/4  
~~7/27/4~~  
~~7/27/4~~

Enter sub-App.  
AR 7/29/4

## TUMOR NECROSIS FACTOR-GAMMA

This application claims benefit under 35 U.S.C. § 119(e) of the filing date of copending U.S. Provisional Application Serial No. 60/074,047, filed on February 9, 1998. Further, this application claims benefit under 35 U.S.C. § 120 as a continuation-in-part of U.S. Application Serial No. 09/131,237, filed on August 7, 1998, which is a continuation-in-part of U.S. Application Serial No. 09/005,020, filed on January 9, 1998, which is a continuation-in-part of U.S. Application Serial No. 08/461,246, filed on June 5, 1995, which is a continuation-in-part of International Application Serial No. PCT/US94/12880, filed on November 7, 1994. Each of the five aforementioned applications are hereby incorporated by reference in their entireties.

### *Field of the Invention*

This invention relates to newly identified polynucleotides, polypeptides encoded by such polynucleotides, the use of such polynucleotides and polypeptides, as well as the production of such polynucleotides and polypeptides. More particularly, the polypeptide of the present invention has been identified as a new member of the tumor necrosis factor family and is hereinafter referred to as "TNF-gamma-alpha". The invention also relates to a protein encoded by a splice variant of the gene encoding TNF-gamma-alpha which is hereinafter referred to as "TNF-gamma-beta". The invention also relates to inhibiting the action of such polypeptides.

### *Background of the Invention*

Human tumor necrosis factors-alpha (TNF-alpha) and beta (TNF-beta or lymphotoxin) are related members of a broad class of polypeptide mediators, which includes the interferons, interleukins and growth factors, collectively called cytokines (Beutler, B. and Cerami, A., Annu. Rev. Immunol., 7:625-655 (1989)).

Tumor necrosis factor (TNF-a and TNF-b) was originally discovered as a result of its anti-tumor activity, however, now it is recognized as a pleiotropic